

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicants: Carl Towns et al.	)	For: Polymers, Their Preparation
	)	and Uses
Serial No. 10/578,895	)	
	)	Group Art Unit: 1786
Filed: November 10, 2004 (Int'l.	)	
Appl. No. PCT/GB2004/004754)	)	Examiner: Brett Alan Crouse
	)	
	)	Confirmation No. 3448

**DECLARATION UNDER 37 C.F.R. § 1.132 OF ANDREW B. HOLMES, Ph.D.**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

I, Andrew B. Holmes, Ph.D., hereby declare as follows:

1. As mentioned in the Declaration under 37 CFR § 1.132 of Andrew B. Holmes, Ph.D. filed April 8, 2011 (hereafter, "the previous Rule 132 Declaration"), I am a co-inventor of the subject matter claimed in the above-identified patent application (hereafter, "the patent application"). I am familiar with the patent application, the June 15, 2011 final action (hereafter, "the final action"), and the documents cited therein.

2. At p. 6, section 6 of the final action, the Examiner explained/asserted that:

Kreuder has been added to the rejection over Kobayashi to provide a showing that the public was in possession of the method of making dihalo-substituted dibenzosilole compounds having the substituents as contemplated by applicant. The reference also teaches that the method taught by Kobayashi would successfully result in the production of dihalo-substituted dibenzosilole compounds having the substituents as contemplated by applicant as taught by Kobayashi. Thus, Kobayashi provides an enabling disclosure to one of ordinary skill in the art.

3. As stated at p. 4, paragraph 11 of the previous Rule 132 Declaration:

The only worked examples reported in Kobayashi for converting compound F (5) into a dihalo-substituted dibenzosilole molecule include the subsequent halogenation of compound F (5) to produce compounds G (6) and H (pp.40-41, Synthetic Example 10) as illustrated by the general synthesis reaction below.

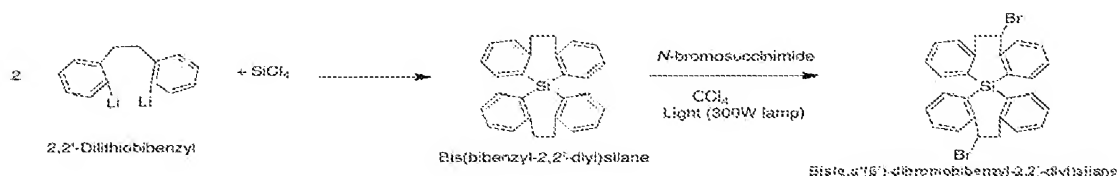


4. Thus, Kobayashi teaches the **aromatic electrophilic bromination** (i.e., substitution of  $\text{Br}^+$  for  $\text{H}^+$  on the aromatic ring) of an electron rich alkoxy-substituted dibenzosilole using N-bromosuccinimide as illustrated in paragraph 3 (above) and in paragraph 11 of the previous Rule 132 Declaration. The use of N-bromosuccinimide as a mild source of  $\text{Br}_2$  (molecular bromine) in aromatic electrophilic brominations is well understood. *See, for example, March, Advanced Organic Chemistry: Reactions, Mechanisms and Structure, 4<sup>th</sup> ed., John Wiley & Sons, New York, p. 532 (1992), which illustrates the bromination of a phenol using a reagent such as N-bromosuccinimide.*<sup>1</sup>

5. As detailed in paragraphs 12-14 of the previous Rule 132 Declaration, the electrophilic bromination reaction allegedly taught by Kobayashi is not enabling for a polymer comprising a dibenzosilole repeat unit having H or an electron withdrawing substituent at the 3- and 6- positions, as recited by formula (I) of claim 1 in the patent application because **halo-desilylation** occurs in the absence of any competing strong electron donating substituent. Thus, Kobayashi does not teach “the production of dihalo-substituted dibenzosilole compounds having the substituents as contemplated by applicant” as asserted by the Examiner. *See final action at pp. 6-7.*

<sup>1</sup> Copy attached as Attachment A.

6. With respect to U.S. Patent No. 6,329,082 to Kreuder et al. (“Kreuder”), the Examiner referenced Example 7 in asserting that Kreuder evidences that Kobayashi has an enabled disclosure. *See* p. 4 of the final action. In Examples 6 and 7, 2,2'-dilithiobibenzyl is prepared by transmetallation of the corresponding 2,2'-dibromobibenzyl with n-butyl-lithium. Reaction of 2,2'-dilithiobibenzyl with silicon tetrachloride then affords bis(bibenzyl-2,2'-diyl)silane.<sup>2</sup> Bis(bibenzyl-2,2'-diyl)silane is then reacted with N-bromosuccinimide in carbon tetrachloride in the presence of a light source to obtain bis( $\alpha,\alpha'$ ( $\beta'$ )-dibromobibenzyl-2,2'-diyl)silane. The reactions are shown below:



7. The above reaction scheme demonstrates that Kreuder teaches **benzylic side chain halogenations** (i.e., introduction of a halogen reagent to replace a hydrogen atom on a carbon attached to an aromatic ring). Further, the reaction conditions of N-bromosuccinimide in carbon tetrachloride in the presence of a light source corroborate that Kreuder teaches benzylic side chain halogenation. *See*, for example, March, pp. 694, 695 (1992).<sup>3</sup>

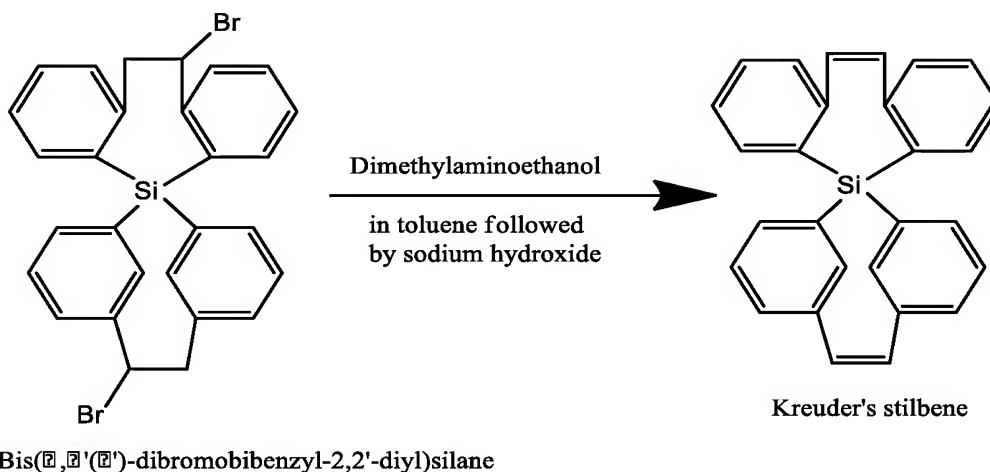
8. In this regard, March teaches that benzylic side chain halogenation is a species of “allylic halogenation.” For example, March teaches that “NBS is also a highly regioselective brominating agent at other positions including positions  $\alpha$  to a carbonyl group, to a  $\text{C}\equiv\text{C}$  triple bond, and **to an aromatic ring (benzylic position).**” *Id.* at p. 695, lines 17-19. Specific reaction conditions are used in allylic halogenations, for example, “[a] non polar solvent is used, most often  $\text{CCl}_4$ .” *Id.* at p. 695, lines 1-2. Further, “[w]ith any reagent [such as N-bromosuccinimide] an initiator is needed; this is usually a peroxide or, less often, uv light.” *Id.* at p. 695,

<sup>2</sup> The structure illustrated at p. 4, section 4 of the final action as corresponding to bis(bibenzyl-2,2'-diyl)silane is incorrect. The correct structure is the middle structure in the scheme illustrated in paragraph 6, above.

<sup>3</sup> Copy attached as Attachment A.

lines 4-5. Based on my expertise and experience, a 300W incandescent tungsten lamp as used in Kreuder is also a suitable initiator. Consistent with the foregoing, when discussing promoting aromatic electrophilic substitution, March teaches that “[s]ince side-chain halogenation is catalyzed by light, the reactions should be run in the absence of light wherever possible.” *Id.* at p. 532, lines 11-13. Finally, March discloses that “the mechanism of allylic bromination is of the free radical type....” *Id.* at p. 695, line 21.

9. In Kreuder Example 7, a combination of bis(bibenzyl-2,2'-diyl)silane and “N-bromosuccinimide in 100 ml of **tetrachloromethane** were heated to boiling **under irradiation** with a 300 W incandescent tungsten lamp.” One of ordinary skill in the art would recognize that these reaction conditions lead to benzylic halogenation as the reactive species is a bromine free radical (not molecular bromine) and thus to the right hand compound in the scheme illustrated in paragraph 6 where the bromine atoms are attached to benzylic carbon atoms in the bridging position and not to the aromatic ring. The bromine atoms must be on the bridging positions as the next stage described by Kreuder is a dehydrohalogenation reaction with diethylaminomethanol and then sodium hydroxide to afford the claimed stilbene (see below).



Thus, like Kobayashi, the combination of Kobayashi and Kreuder also does not teach “the method of making dihalo-substituted dibenzosilole compounds having the substituents as contemplated by applicant” as asserted by the Examiner. *See* final action at p. 7.

10. At p. 7 of the final action, the Examiner explained/asserted that:

Kreuder has been added to the rejection over Roberts to provide a showing that the public was in possession of the method of making dihalo-substituted dibenzosilole compounds having the substituents as contemplated by applicant.

11. As stated at pp.6-7, paragraph 18 of the previous Rule 132 Declaration:

...Roberts only teaches preparation of carbon bridged materials and provides no teachings regarding the synthesis of a polymer comprising a dibenzosilole repeat unit, much less a polymer comprising a dibenzosilole repeat unit having H or an electron withdrawing substituent at the 3- and 6- positions, as recited by formula (I) of claim 1 in the patent application. There is no disclosure in Roberts regarding how Si atoms are introduced into the dibenzosiloles shown as compounds XXXIV and LIV. Consequently, Roberts is not enabling for a polymer comprising a dibenzosilole repeat unit having H or an electron withdrawing substituent at the 3- and 6- positions, as recited by formula (I) of claim 1 in the patent application.

12. Kreuder does not remedy any of the previously noted deficiencies in Roberts. Thus, the combination of Roberts and Kreuder does not teach “the method of making dihalo-substituted dibenzosilole compounds having the substituents as contemplated by applicant” as asserted by the Examiner. *See* final action at p. 7.

13. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. §1001 and that such willful false statements may jeopardize the validity of the above-referenced patent application and any patent issued therefrom.

Date: September 14th, 2011

By

*Andrew B. Holmes*

Andrew B. Holmes, Ph.D.

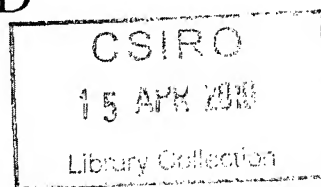
# ORGANIC CHEMISTRY

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MECHANISMS, AND  
STRUCTURE

**FOURTH EDITION**

**Jerry March**

Professor of Chemistry  
Adelphi University



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ATTACHMENT A

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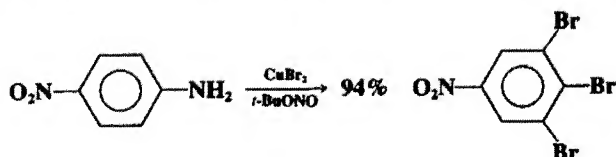
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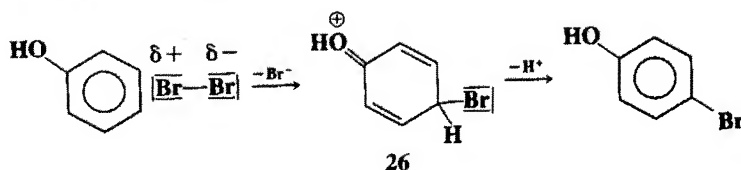
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to the  $\text{OH}_2^+$  group, which should be meta-directing because of its positive charge. Bromination and the Sandmeyer reaction (4-25) can be carried out in one laboratory step by treatment of an aromatic primary amine with  $\text{CuBr}_2$  and *t*-butyl nitrite, e.g.,<sup>182</sup>



Other reagents have been used, among them  $\text{HOCl}$ ,<sup>183</sup>  $\text{HOBr}$ , and N-chloro and N-bromo amides (especially N-bromosuccinimide and tetraalkylammonium polyhalides<sup>184</sup>). In all but the last of these cases the reaction is catalyzed by the addition of acids. Dibromoisocyanuric acid in  $\text{H}_2\text{SO}_4$  is a very good brominating agent<sup>185</sup> for substrates with strongly deactivating substituents.<sup>186</sup> Two particularly powerful reagents consist of (1)  $\text{S}_2\text{Cl}_2$  and  $\text{AlCl}_3$  in sulfuryl chloride ( $\text{SO}_2\text{Cl}_2$ ) (the *BMC reagent*)<sup>187</sup> and (2) dichlorine oxide  $\text{Cl}_2\text{O}$  and a strong acid such as sulfuric.<sup>188</sup> If the substrate contains alkyl groups, side-chain halogenation (4-1) is possible with most of the reagents mentioned, including chlorine and bromine. Since side-chain halogenation is catalyzed by light, the reactions should be run in the absence of light wherever possible.

For reactions in the absence of a catalyst, the attacking entity is simply  $\text{Br}_2$  or  $\text{Cl}_2$  that has been polarized by the ring.<sup>189</sup>



Evidence for molecular chlorine or bromine as the attacking species in these cases is that acids, bases, and other ions, especially chloride ion, accelerate the rate about equally, though if chlorine dissociated into  $\text{Cl}^+$  and  $\text{Cl}^-$ , the addition of chloride should decrease the rate and the addition of acids should increase it. The conjugate base of **26** (4-bromo-2,5-cyclohexadienone) has been detected spectrally in the aqueous bromination of phenol.<sup>190</sup>

When a Lewis-acid catalyst is used with chlorine or bromine, the attacking entity may be  $\text{Cl}^+$  or  $\text{Br}^+$ , formed by  $\text{FeCl}_3 + \text{Br}_2 \rightarrow \text{FeCl}_3\text{Br}^+ + \text{Br}^-$ , or it may be  $\text{Cl}_2$  or  $\text{Br}_2$ , polarized by the catalyst. With other reagents, the attacking entity in brominations may be  $\text{Br}^+$  or a species such as  $\text{H}_2\text{OBr}^+$  (the conjugate acid of  $\text{HOBr}$ ), in which  $\text{H}_2\text{O}$  is a carrier of  $\text{Br}^+$ .<sup>191</sup>

<sup>182</sup>Doyle; Van Lente; Mowat; Fobare *J. Org. Chem.* **1980**, *45*, 2570.

<sup>183</sup>For the use of calcium hypochlorite, see Nwaukwa; Keehn *Synth. Commun.* **1989**, *19*, 799.

<sup>184</sup>See Kajigaeshi; Moriwaki; Tanaka; Fujisaki; Kakinami; Okamoto *J. Chem. Soc., Perkin Trans. 1* **1990**, 897, and other papers in this series.

<sup>185</sup>Nitrobenzene is pentabrominated in 1 min with this reagent in 15% oleum at room temperature.

<sup>186</sup>Gottardi *Monatsh. Chem.* **1968**, *99*, 815, **1969**, *100*, 42.

<sup>187</sup>Ballester; Molinet; Castañer *J. Am. Chem. Soc.* **1960**, *82*, 4254; Andrews, Glidewell; Walton *J. Chem. Res.* (S) **1978**, 294.

<sup>188</sup>Marsh; Farnham; Sam; Smart *J. Am. Chem. Soc.* **1982**, *104*, 4680.

<sup>189</sup>For reviews of the mechanism of halogenation, see de la Mare, Ref. 171; de la Mare; Swedlund, in Patai *The Chemistry of the Carbon-Halogen Bond*, pt. 1; Wiley: New York, 1973; pp. 490-536; Taylor, in Bamford; Tipper, Ref. 1, pp. 83-139; Berliner *J. Chem. Educ.* **1966**, *43*, 124-133. See also Schubert; Dial *J. Am. Chem. Soc.* **1975**, *97*, 3877; Keefer; Andrews *J. Am. Chem. Soc.* **1977**, *99*, 5693; Briggs; de la Mare; Hall *J. Chem. Soc., Perkin Trans. 2*

With  $\text{HOCl}$  in water the attacking entity is generally  $\text{AcOCl}$ . All these reactions are highly doubtful that  $\text{Cl}^+$  is a significant attacking entity at these ranges (as in 1-35) to give a particular isomer predominates.<sup>193</sup>

$\text{FeCl}_3$  itself, and also  $\text{CuCl}_2$ , are used. The electrophile might be  $\text{FeCl}_4^+$  or  $\text{CuCl}_2$  by a free-radical mechanism.

When chlorination or bromination is directed by ortho-para-directing groups, the reaction is not complete by the  $\text{SEI}$  mechanism, e.g. benzene.<sup>198</sup>

**2. Iodine.** Iodine is the most active electrophile for active substrates, an oxidizing electrophile.<sup>200</sup> Examples of active substrates are  $\text{H}_2\text{O}_2$ .<sup>201</sup>  $\text{ICl}$  is a better reagent than  $\text{I}_2$ . Iodine has been used have been  $\text{IF}$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_3$ ),  $\text{ICl}$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_3$ ),  $\text{ICl}_3$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_3$ ),  $\text{ICl}_4^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_4^-$ ),  $\text{ICl}_5$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_5$ ),  $\text{ICl}_6^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_6^-$ ),  $\text{ICl}_7^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_7^-$ ),  $\text{ICl}_8^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_8^-$ ),  $\text{ICl}_9^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_9^-$ ),  $\text{ICl}_{10}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{10}^-$ ),  $\text{ICl}_{11}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{11}^-$ ),  $\text{ICl}_{12}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{12}^-$ ),  $\text{ICl}_{13}^-$  (prepared from  $\text{I}_2$  and  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),  $\text{ICl}_{100}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{100}^-$ ),  $\text{ICl}_{101}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{101}^-$ ),  $\text{ICl}_{102}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{102}^-$ ),  $\text{ICl}_{103}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{103}^-$ ),  $\text{ICl}_{104}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{104}^-$ ),  $\text{ICl}_{105}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{105}^-$ ),  $\text{ICl}_{106}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{106}^-$ ),  $\text{ICl}_{107}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{107}^-$ ),  $\text{ICl}_{108}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{108}^-$ ),  $\text{ICl}_{109}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{109}^-$ ),  $\text{ICl}_{110}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{110}^-$ ),  $\text{ICl}_{111}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{111}^-$ ),  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$\text{ICl}_{124}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{124}^-$ ),  $\text{ICl}_{125}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{125}^-$ ),  $\text{ICl}_{126}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{126}^-$ ),  $\text{ICl}_{127}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{127}^-$ ),  $\text{ICl}_{128}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{128}^-$ ),  $\text{ICl}_{129}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{129}^-$ ),  $\text{ICl}_{130}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{130}^-$ ),  $\text{ICl}_{131}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{131}^-$ ),  $\text{ICl}_{132}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{132}^-$ ),  $\text{ICl}_{133}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{133}^-$ ),  $\text{ICl}_{134}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{134}^-$ ),  $\text{ICl}_{135}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{135}^-$ ),  $\text{ICl}_{136}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{136}^-$ ),  $\text{ICl}_{137}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{137}^-$ ),  $\text{ICl}_{138}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{138}^-$ ),  $\text{ICl}_{139}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{139}^-$ ),  $\text{ICl}_{140}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{140}^-$ ),  $\text{ICl}_{141}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{141}^-$ ),  $\text{ICl}_{142}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{142}^-$ ),  $\text{ICl}_{143}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{143}^-$ ),  $\text{ICl}_{144}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{144}^-$ ),  $\text{ICl}_{145}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{145}^-$ ),  $\text{ICl}_{146}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{146}^-$ ),  $\text{ICl}_{147}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{147}^-$ ),  $\text{ICl}_{148}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{148}^-$ ),  $\text{ICl}_{149}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{149}^-$ ),  $\text{ICl}_{150}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{150}^-$ ),  $\text{ICl}_{151}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{151}^-$ ),  $\text{ICl}_{152}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{152}^-$ ),  $\text{ICl}_{153}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{153}^-$ ),  $\text{ICl}_{154}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{154}^-$ ),  $\text{ICl}_{155}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{155}^-$ ),  $\text{ICl}_{156}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{156}^-$ ),  $\text{ICl}_{157}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{157}^-$ ),  $\text{ICl}_{158}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{158}^-$ ),  $\text{ICl}_{159}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{159}^-$ ),  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$\text{ICl}_{172}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{172}^-$ ),  $\text{ICl}_{173}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{173}^-$ ),  $\text{ICl}_{174}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{174}^-$ ),  $\text{ICl}_{175}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{175}^-$ ),  $\text{ICl}_{176}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{176}^-$ ),  $\text{ICl}_{177}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{177}^-$ ),  $\text{ICl}_{178}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{178}^-$ ),  $\text{ICl}_{179}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{179}^-$ ),  $\text{ICl}_{180}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{180}^-$ ),  $\text{ICl}_{181}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{181}^-$ ),  $\text{ICl}_{182}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{182}^-$ ),  $\text{ICl}_{183}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{183}^-$ ),  $\text{ICl}_{184}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{184}^-$ ),  $\text{ICl}_{185}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{185}^-$ ),  $\text{ICl}_{186}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{186}^-$ ),  $\text{ICl}_{187}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{187}^-$ ),  $\text{ICl}_{188}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{188}^-$ ),  $\text{ICl}_{189}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{189}^-$ ),  $\text{ICl}_{190}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{190}^-$ ),  $\text{ICl}_{191}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{191}^-$ ),  $\text{ICl}_{192}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{192}^-$ ),  $\text{ICl}_{193}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{193}^-$ ),  $\text{ICl}_{194}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{194}^-$ ),  $\text{ICl}_{195}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{195}^-$ ),  $\text{ICl}_{196}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{196}^-$ ),  $\text{ICl}_{197}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{197}^-$ ),  $\text{ICl}_{198}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{198}^-$ ),  $\text{ICl}_{199}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{199}^-$ ),  $\text{ICl}_{200}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{200}^-$ ),  $\text{ICl}_{201}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{201}^-$ ),  $\text{ICl}_{202}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{202}^-$ ),  $\text{ICl}_{203}^-$  (prepared from  $\text{I}_2$  and  $\text{FeCl}_{203}^-$ ),  $\text{ICl}_{204}^-$  (prepared from  $\text{$



TABLE 14.4 Some *D* values<sup>106</sup>

Bond	<i>D</i>	
	kcal/mol	kJ/mol
H-F	136	570
H-Cl	103	432
H-Br	88	366
H-I	71	298
F-F	38	159
Cl-Cl	59	243
Br-Br	46	193
I-I	36	151
CH <sub>3</sub> -F	108	452
CH <sub>3</sub> -Cl	85	356
CH <sub>3</sub> -Br	70	293
CH <sub>3</sub> -I	57	238

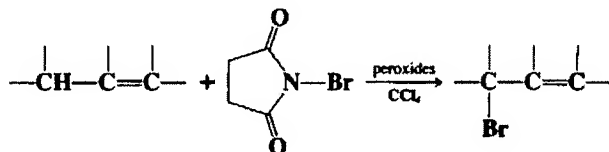
to be  $F_2 > Cl_2 > Br_2 > I_2$  is the decreasing strength of the HX bond in the order  $HF > HCl > HBr > HI$ . The increased reactivity of secondary and tertiary positions is in accord with the decrease in *D* values for R—H in the order primary > secondary > tertiary (Table 5.3). (Note that for chlorination step 1 is exothermic for practically all substrates other than CH<sub>4</sub>, since most other aliphatic C—H bonds are weaker than those in CH<sub>4</sub>.)

Bromination and chlorination of alkanes and cycloalkanes can also take place by an electrophilic mechanism if the reaction is catalyzed by AgSbF<sub>6</sub>.<sup>112</sup> Direct chlorination at a vinylic position by an electrophilic mechanism has been achieved with benzeneseleninyl chloride PhSe(O)Cl and AlCl<sub>3</sub> or AlBr<sub>3</sub>.<sup>113</sup> However, while some substituted alkenes give high yields of chloro substitution products, others (such as styrene) undergo addition of Cl<sub>2</sub> to the double bond (5-26).<sup>113</sup> Electrophilic fluorination has already been mentioned (p. 690).

OS II, 89, 133, 443, 549; III, 737, 788; IV, 807, 921, 984; V, 145, 221, 328, 504, 635, 825; VI, 271, 404, 715; VII, 491; 65, 68.

#### 4-2 Allylic Halogenation

##### Halogenation or Halo-de-hydrogenation



This reaction is a special case of 4-1, but is important enough to be treated separately.<sup>114</sup> Olefins can be halogenated in the allylic position by a number of reagents, of which N-bromosuccinimide (NBS)<sup>115</sup> is by far the most common. When this reagent is used, the

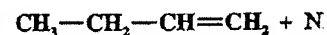
<sup>112</sup>Olah; Renner; Schilling; *Mo J. Am. Chem. Soc.* 1973, 95, 7686. See also Olah; Wu; Farooq *J. Org. Chem.* 1989, 54, 1463.

<sup>113</sup>Comins; Sato; Yoshida *Bull. Chem. Soc. Jpn.* 1988, 61, 110.

#### REACTION 4-2

reaction is known as *Wohl-Z* CCl<sub>4</sub>. Other N-bromo amides nation has been carried out, sulfonamide,<sup>116</sup> or *t*-butyl hyp usually a peroxide or, less oft

The reaction is usually quit However, when the allylic radi take place, so that mixtures o



When a double bond has tw secondary position is substitu tertiary hydrogen is not clear been performed.<sup>118</sup> It is possit the electron-withdrawing natr side of the double bond rathe

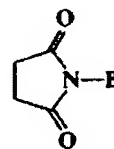
NBS is also a highly regio: sitions α to a carbonyl group position). When both a doubl position is α to the triple bon

That the mechanism of all by Dauben and McCoy,<sup>121</sup> w initiators and inhibitors and in is present. Subsequent work in the substrate is the bromine a it is formed, the main propag

Step 1

Step 2

The source of the Br<sub>2</sub> is a 1 step 1:



The function of the NBS is concentration and to use up

<sup>116</sup>Theilacker; Wessel *Liebigs Ann.*

<sup>117</sup>Walling; Thaler *J. Am. Chem. Soc.*

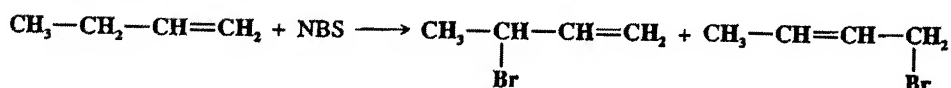
<sup>118</sup>Dauben; McCoy *J. Org. Chem.*

<sup>119</sup>Ucciani; Naudet *Bull. Soc. Chim.*

<sup>120</sup>Peiffer *Bull. Soc. Chim. Fr.* 19

reaction is known as *Wohl-Ziegler bromination*. A nonpolar solvent is used, most often  $\text{CCl}_4$ . Other N-bromo amides have also been used. To a much lesser extent, allylic chlorination has been carried out, with N-chlorosuccinimide, N-chloro-N-cyclohexylbenzenesulfonamide,<sup>116</sup> or *t*-butyl hypochlorite.<sup>117</sup> With any reagent an initiator is needed; this is usually a peroxide or, less often, uv light.

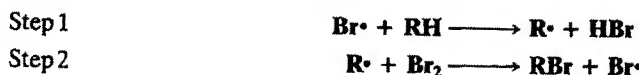
The reaction is usually quite specific at the allylic position and good yields are obtained. However, when the allylic radical intermediate is unsymmetrical, allylic rearrangements can take place, so that mixtures of both possible products are obtained, e.g.,



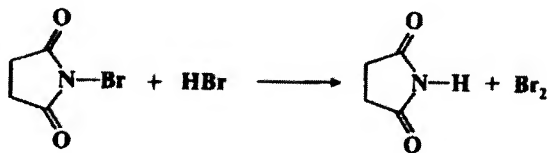
When a double bond has two different allylic positions, e.g.,  $\text{CH}_3\text{CH}=\text{CHCH}_2\text{CH}_3$ , a secondary position is substituted more readily than a primary. The relative reactivity of tertiary hydrogen is not clear, though many substitutions at allylic tertiary positions have been performed.<sup>118</sup> It is possible to brominate both sides of the double bond.<sup>119</sup> Because of the electron-withdrawing nature of bromine, the second bromine substitutes on the other side of the double bond rather than  $\alpha$  to the first bromine.

NBS is also a highly regioselective brominating agent at other positions, including positions  $\alpha$  to a carbonyl group, to a  $\text{C}\equiv\text{C}$  triple bond, and to an aromatic ring (benzylic position). When both a double and a triple bond are in the same molecule, the preferred position is  $\alpha$  to the triple bond.<sup>120</sup>

That the mechanism of allylic bromination is of the free-radical type was demonstrated by Dauben and McCoy,<sup>121</sup> who showed that the reaction is very sensitive to free-radical initiators and inhibitors and indeed does not proceed at all unless at least a trace of initiator is present. Subsequent work indicated that the species that actually abstracts hydrogen from the substrate is the bromine atom. The reaction is initiated by small amounts of  $\text{Br}^\bullet$ . Once it is formed, the main propagation steps are



The source of the  $\text{Br}_2$  is a fast ionic reaction between NBS and the HBr liberated in step 1:



The function of the NBS is therefore to provide a source of  $\text{Br}_2$  in a low, steady-state concentration and to use up the HBr liberated in step 1.<sup>122</sup> The main evidence for this

<sup>116</sup>Theilacker; Wessel *Liebigs Ann. Chem.* **1967**, 703, 34.

<sup>117</sup>Walling; Thaler *J. Am. Chem. Soc.* **1961**, 83, 3877.

<sup>118</sup>Dauben; McCoy *J. Org. Chem.* **1959**, 24, 1577.

<sup>119</sup>Ucciani; Naudet *Bull. Soc. Chim. Fr.* **1962**, 871.

<sup>120</sup>Peiffer *Bull. Soc. Chim. Fr.* **1963**, 537.